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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/645,415	08/24/2000	David G. Bermudes	8002-059-999	3240

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EXAMINER	
SHUKLA, RAM R	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/28/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/645,415	Applicant(s) BERMUDES ET AL.	
	Examiner Ram Shukla	Art Unit 1632	

-- Th MAILING DATE of this communication appears on th cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2002* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-99* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

1. Claims 1-99 are pending in the instant application.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 3-12, 14, 15, 25, 27-36, 38, 39, 48, 50-59, 61, and 62, 71, 73-85, drawn to an attenuated tumor targeted bacteria comprising one or more nucleic acid molecules encoding a primary effector molecule, classified in class 435, subclass 252.3.

II. Claims 2,3-14,16, 26-38, 40, 49-61, 63, 72-84, 86, drawn to an attenuated tumor targeted bacteria comprising one or more nucleic acid molecules encoding one or more primary effector molecules and one or more secondary effector molecule, classified in class 435, subclass 252.3.

III. Claims 17, 20, 22-24 and 41, 44-47, 64, 67, 69, 70, 87, 90, 92, and 93, drawn to an attenuated tumor targeted bacteria comprising one or more nucleic acid molecules encoding one or more fusion proteins comprising a signal sequence and a primary effector molecule, classified in class 435, subclass 252.3.

IV. Claims 17-24 and 41-47, 65-70, and 88-93, drawn to an attenuated tumor targeted bacteria comprising one or more nucleic acid molecules encoding one or more fusion proteins comprising a ferry peptide and an effector molecule, classified in class 435, subclass 252.3.

V. Claims ~~94~~ 95, drawn to fusion protein comprising an Omp-A like protein and an effector molecule, classified in class 530, subclass 350.

VI. Claims ~~95-99~~ 96-99, drawn to fusion protein comprising a signal sequence, a ferry peptide and an effector molecule, classified in class 530, subclass 350.

3. The inventions of Groups I and II encompass the limitations of the claim 3-12, 14, 27-26, 38, 50-59, and 73-84. Should any of these groups be elected for prosecution, the invention of claim 3-12, 14, 27-26, 38, 50-59, and 73-84 would be examined to the extent it encompasses the claimed invention.

4. The inventions of Groups III and IV encompass the limitations of the claim 17, 20, 22-24, 41, 44-47,69, 70, 90, 92, and 93. Should any of these groups be elected for prosecution, the invention of claim 17, 20, 22-24, 41, 44-47,69, 70, 90, 92, and 93 would be examined to the extent it encompasses the claimed invention.

5. This application contains claims directed to the following patentably distinct species of the claimed invention:

one for each family

Claims 3, 5, 7, 9, and 11:

TNF family member, anti-angiogenic factor, tumor inhibitory enzyme, hemolysin, verotoxin, CNF-1, CNF2, or PMT.

Claims 4, 28, 51, and 74:

TNF-α, TRAIL, TRANCE, TWEAK, CD40L, LT-α, LT-β, OX4OL, CD40L, FasL, CD27L, CD30L, 4-1BBL, APRIL, LIGHT, TL1, TNFSF16, TNFSF17, or AITR-L.

Claims 6, 30, 53, and 76:

Endostatin, angiostatin, anti-angiogenic antithrombin III, the 29 kDa N-terminal and 140 kDa C-terminal proteolytic fragments of fibronectin, a uPA receptor antagonist, the 16 kDa proteolytic fragment of prolactin, the 7.8 kDa proteolytic fragment of platelet factor-4, the anti-angiogenic 24 amino acid fragment of platelet factor-4, the anti-angiogenic factor designated 13.40, the anti-angiogenic 22 amino acid peptide fragment of thrombospondin I, the anti-angiogenic 20 amino acid peptide fragment of SPARC, RGD, and NGR containing peptides, the small anti-angiogenic peptides of laminin, fibronectin, procollagen and EGF, and peptide antagonists of integrin $\alpha_v\beta_3$, or VEGF receptor.

Claims 8, 32, 55, and 78 :

ColE1, ColE1a, ColE1b, ColE2, ColE3, ColE4, ColE5, ColE6, ColE7, ColE8, ColE9, Colicin A, Colicin K, Colicin L, Colicin M, Cloacin DF13, pesticin A1122, staphylococcin 1580, butyricin 7423, pyocin R1 or AP41, megacin A-216, vibriocin, or microcin M15.

Claim 13, 37, 60, and 83:

An immunomodulating agent, an ant-tumor protein, a pro-drug converting enzyme, an antisense molecule, ribozyme, or an antigen.

Claim 21, 45, 68, 91, and 98:

HIV TAT protein, the antennapedia homeodomain (penetraxin), kaposi FGF membrane targeting sequence, HSV VP22, hexahistidine, hexalysine, or hexaarginine.

Claim 10, 34, 57, and 80:

Methionase, asparaginase, lipase, phospholipase, protease, DNAse or glycosidase.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Claims that are generic are indicated as above.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. The inventions are distinct, each from the other because of the following reasons:

Inventions of the groups I and II are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination (group II) as claimed does not require the particulars of the subcombination as claimed for delivering a protein to a bacteria and as a pharmaceutical composition in treating a tumor since the secondary effector molecules (such as the immunomodulating agent, anti-tumor protein etc) would

produce the treatment effect. The subcombination of the groups I has separate utility because the bacteria comprising a primary effector molecule (such as TNF alpha) can be used as a pharmaceutical composition or in the treatment method alone or for producing proteins encoded by the polynucleotides comprised in the bacteria.

Inventions of the groups III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions directed to bacteria comprising a nucleic acid encoding fusion proteins comprising a signal peptide and an effector molecule or a ferry peptide and an effector molecule would have different sequence structure and would have different modes of operation. For example, a signal peptide will direct the bacteria to a particular compartment of a cell whereas a ferry peptide would affect the function of a protein based on its target molecule.

Inventions of the groups V and VI are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the fusion protein of group VI can effect a treatment even without the presence of a signal peptide, such as OmpA-like protein. The subcombination has separate utility such as for producing an antibody that can be used in detecting the presence of the effector molecule in a cell or a sample.

Inventions III and V are related as apparatus and product made. The inventions in this relationship are distinct if either or both of the following can be shown: (1) that the apparatus as claimed is not an obvious apparatus for making the product and the apparatus can be used for making a different product or (2) that the product as claimed can be made by another and materially different apparatus (MPEP § 806.05(g)). In this case the fusion protein of group V can be

produced by expressing an expression construct in a eukaryotic cell. Alternatively, the bacteria can be used for producing different proteins, other than the fusion protein.

Inventions of the groups I & II are unrelated to the inventions of the groups III and IV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions the sequence structure of the proteins produced by the bacteria of the invention of the groups I and II are different from the sequence structure of the invention of the proteins produced by the bacteria of groups III and IV. Furthermore, the proteins produced by the bacteria of the groups III and IV would have different mode of operation than those of the proteins produced by the bacteria of groups I and II because the proteins of groups III and IV would be targeted to a specification location.

7. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art shown by their different classification and their recognized divergent subject matter, and because each invention requires a separate, non-coextensive search, restriction for examination purposes as indicated is proper.

8. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.

Ram R. Shukla

RAM R. SHUKLA, PH.D
PATENT EXAMINER